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Review

Fatty acid-binding proteins as plasma markers of tissue injury

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Abstract

Background: One of the novel and promising plasma markers for detection of tissue injury is the family of 15 kDa cytoplasmic fatty acid-binding proteins of which various tissue-specific types occur.
Aims and Objectives: The present status of heart-type fatty acid-binding protein (H-FABP) as a diagnostic and prognostic marker for acute and chronic cardiac injury, as well as the preliminary diagnostic use of other types of FABP for detecting injury in other organs, is reviewed.
Methods: This review is based on an overview of the literature on clinical diagnostics of various forms of organ injury, and uses additional literature on physiological aspects relevant for the interpretation of plasma marker concentrations.
Results: H-FABP not only proves to be an excellent early marker for cardiac injury in acute coronary syndromes, but also allows detection of minor myocardial injury in heart failure and unstable angina. Preliminary results indicate that sensitivity, rule-out power and prognostic value of H-FABP in cardiac injury surpass the performance of the standard early marker myoglobin. The liver only contains liver-type FABP (L-FABP), but co-expression of H-FABP and L-FABP occurs in the kidney. Similarly, intestinal-type FABP (I-FABP) and L-FABP are found in intestines, and brain-type FABP (B-FABP) and H-FABP occur in the brain. Preliminary but promising applications of these proteins have been demonstrated for liver rejection, viability selection of kidneys from non-heart-beating donors (NHBD), inflammatory and ischemic bowel disease, traumatic brain injury and in the prevention of muscle injury in trained athletes.
Conclusions: Further study of the diagnostic and prognostic use of various FABP types is warranted, but their clinical application will require further commercialization of automated and rapid assays.

Keywords: FABP; Tissue injury; ELISA; Myocardial infarction; Point-of-care testing

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Contents

1. Introduction

The appearance in plasma of cellular proteins released after tissue injury, or produced by malignant cells, commonly referred to as biochemical markers, is gaining more and more interest as being important in the management of patients with tissue injury due to acute ischemia/reperfusion, neurological disorders, cancer, organ rejection or trauma.

One of the promising new biomarker proteins is the fatty acid-binding protein (FABP). This relatively small (15 kDa) cytoplasmic protein is abundantly expressed in tissues with an active fatty acid metabolism like heart and liver [1,2]. Presently, nine distinct types have been identified, with each type showing a characteristic pattern of tissue distribution and a stable intracellular half-life of 2–3 days [1]. These FABP types are named after the tissue in which they were first identified and belong to a multigene family of intracellular lipid-binding proteins [1,3,4]. Their tertiary structure resembles a clam shell in which the ligand is bound between the two halves of the clam by interaction with specific amino acid residues within the binding pocket, the so-called β-barrel [3,5]. The primary function of FABP is the facilitation of intracellular long-chain fatty acid transport [6], while other functions include regulation of gene expression by mediating fatty acid signal translocation to peroxisome proliferator activated receptors (PPARs) [7] and putative protection of cardiac myocytes against the detergent-like effects of locally high concentrations of long-chain fatty acids, especially during ischemia [1,8]. The cellular expression of FABPs is regulated primarily at the transcriptional level and is responsive to changes in lipid metabolism as induced by (patho)physiological and pharmalogical stimuli like ischemia [9], endurance training [10], diabetes [11,12], hypertrophy [13,14] and hypolipidemic drugs [15].

When evaluating FABP as clinical tissue injury marker, we have to take into account that after cell damage small proteins diffuse more rapidly than large proteins through the interstitial space via endothelial clefts into vascular space. The size of these endothelial clefts is variable, from large clefts in the liver to smaller pores in the heart, the skeletal muscle and finally to almost complete impermeability in the brain (blood–brain barrier). As a result, the diffusion rate of the released proteins into the circulation also differs. Therefore, the time of appearance of these marker proteins in plasma is not only dependent on the time course of the disease, but also on the molecular size